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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,388	04/14/2005	Stephen Martin Courtney	Cell-0286	1693

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WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE, 46TH FLOOR
1650 MARKET STREET
PHILADELPHIA, PA 19103

EXAMINER	
CHU, YONG LIANG	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 01/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/506,388	COURTNEY ET AL.	
	Examiner	Art Unit	
	Yong Chu	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15,16 and 23-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-13,15 and 16* is/are allowed.

6)☒ Claim(s) *23-29* is/are rejected.

7)☒ Claim(s) *25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *15 September 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-13, and 15-16 have been amended by preliminary amendment filed on April 14, 2005. Claims 14, and 17-22 have been cancelled by preliminary amendment filed on April 14, 2005. Claims 23-29 have been added in by preliminary amendment filed on April 14, 2005. Therefore, claims 1-13, 15-16, and 23-29 are currently pending in this application.

Information Disclosure Statement

Applicant's Information Disclosure Statement, filed on September 15, 2005 has been considered. Please refer to Applicant's copies of the 1449 submitted herewith.

Priority

This application is a national phase application of PCT Patent Application No. PCT/GB03/00926 filed on March 6, 2003, which claims the benefit of foreign priority to UK 0205256.1 filed on March 6, 2002.

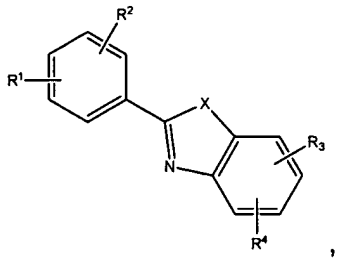
Response to Restriction

During a telephone conversation with Applicants' representative, Jane Inglese, 10 January 2006, The Examiner's suggestion of dropping or/and amending some of the method-to-use claims due to lack of enablement was not accepted by Applicants.

Status of the Claims

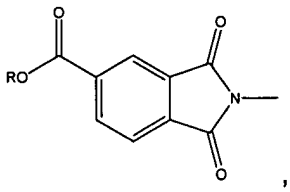
Claims 1-13, 15-16, and 23-29 are currently pending in this application.

The scope of the invention of the elected subject matter is as follows:

Compounds of formula (I), 

, depicted in claim 1, wherein:

X is O or S;

R_1 is represented by formula (II) 

, wherein **R** is H, C_1-C_6 alkyl;

R_2 is H, or OR^5, wherein R^5 is H, or C_1-C_6 alkyl;

R_3 is H or C_1-C_6 alkyl;

R_4 is the group as defined in claim 1 except NHCOR^7, $NHSO_2R^9$ not included;

R^6 – R^{11} are groups as defined in claim 1;

P is 0, 1, or 2.

As a result of the amendment and the corresponding scope of the invention identified supra, the remaining subject matter of claims 1-13, and 15-16 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being drawn to non-elected inventions. The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations. This recognized chemical diversity of the functional groups can

be seen by the various classification of these functional groups in the U.S. classification system, e.g. $NHCOR^7$ is patentably different from hydrogen, alkyl, OR^{10}, and COR^6. In addition, a reference, which anticipates one group, would not render obvious the other.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for inhibiting heparanase activity in **a patient** suffering from a disease or disorder in which heparanase activity plays a role. As described in the specification, there are many diseases associated with heparanase, and the treatment for these diseases involves different pharmacology process, and the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 24, 25 (in part), and 26-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the treatment of most of the claimed cancers (except melanoma in claim 25), angiogenesis, angiogenesis related disorders, inflammatory diseases, autoimmune disorders, cardiovascular diseases, or rental disorders.

As described in the specification, the treatments for cancers, angiogenesis, angiogenesis related disorders, inflammatory diseases, autoimmune disorders, cardiovascular diseases, or rental disorders involve different pharmacology process, and the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

As stated in MPEP 2164.01(a), "there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The eight Wands factors are applied to Claims 23-29 of the present inventions below:

The Nature of the Invention

The nature of the invention in claims 23-29 are a method for inhibiting heparanase activity in a patient suffering from a disease or disorder in which

heparanase activity plays a role or a treatment of cancer, angiogenesis, angiogenesis related disorders, inflammatory diseases, autoimmune disorders, cardiovascular diseases, or rental disorders.

The level of skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

The predictability or lack thereof in the art

Because of high level of unpredictability associated with treatment of certain diseases such as leukemia, cervical cancer or multiple sclerosis, a greater amount of evidentiary support is needed to fully satisfy the requirement of 35 U.S.C 112, first paragraph. It is noted that pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of

these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The specification discloses methods of Heparanase and Angiogenesis assay to measure the inhibition potencies (IC_{50}) of Heparanase and Angiogenesis the various compounds of formula (I) in claim 1. However, there is no description in specification on how to use compounds for treating the diseases. The specification is short of data (animal models, in vitro, or in vivo testing) in regards to the treatment of said diseases.

The presence or absence of working examples

A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that compounds fall within the scope of a claim will posses the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724. The instant specification does not provide any example for treating diseases as being claimed. One of the research results by Parish *et al.* Cancer Research 59 (1999), pp 3433-3441 disclosed sulfated Oligosaccharide-based Inhibitors of primary tumor growth of the rat mammary adenocarcinoma 13762 MAT cells (see Fig. 6 page 3439). The inhibitor is oligosaccharide-based, which is very different in terms of chemical and physical prosperities from instant claimed compounds which are phthalimide carboxylic acid

oligosaccharide-based compounds show only effectiveness on solid tumor in the animal model.

The breadth of the claims

As defined the claims read on treating diseases associated with Heparanase, such as cancers, angiogenesis, angiogenesis related disorders, inflammatory diseases, autoimmune disorders, cardiovascular diseases, or rental disorders, which is broader than the enabling disclosure.

The quantity of experimentation needed

Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the art would be burdened with undue "experimentation study" to determine whether the claimed compounds would treat diseases such as leukemia. Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which compounds would treat leukemia for

example by the method encompassed in the instant claims, with no assurance of success.

Objections

Claim 25 (in part with the method of treatment of melanoma) is objected to as being dependent upon a rejected base claim 24 (the treatment of cancer, angiogenesis,...), but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 1-13, and 15-16 are allowed.

Claims 23, 24, 25 (in part), and 26-29 are rejected.

Claim 25 (in part) is objected.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu whose telephone number is 571-272-5759. The examiner can normally be reached on 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yong Chu, Ph.D.
Patent Examiner
Art Unit 1626

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

Joseph M. McKane
Supervisory Patent Examiner
Art Unit 1626